# "SYNTHESIS, CHARACTERIZATION OF NOVEL HETEROCYCLIC COMPOUNDS USING KETENE THIOACETALS AND EVALUATION OF PHYSICOCHEMICAL PROPERTIES WITH BIOLOGICAL ACTIVITIES"

SHORT RESUME OF THE PLAN PROPOSED FOR INVESTIGATION FOR Ph.D. DEGREE UNDER THE FACULTY OF SCIENCE.

To be submitted to

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## 1. Introduction:

Heterocycles were most frequently studied liable unit in pharmaceutical chemistry during last 3-4 recent decade. The biological importance of this class of compound is due to presence of hetero atom like oxygen, nitrogen and sulphur in their ring structure. Heterocycles play vital role in nature and are of great impact to life; there are structural subunits present in natural product like antibiotics, vitamins, hormones etc. Therefore, these class of compounds have attracted to design new compounds having biological importance.

Heterocyclic compounds show broad existence in nature, particularly in biological system like nucleic acids, hemoglobin, plant, hormones and enzymes. Organic synthesis is one of the special branches in chemical synthesis and is concerned with the construction of organic compounds by reaction. It is believed to be one of the most vital roles in organic chemistry because of the organic molecules used to contain higher level of complexity compared to pure inorganic compounds. So far, organic synthesis plays very significant role in many sectors as pharmaceuticals, in agriculture and other field.

## 2. Review of Literature and Development in the subject (Previous work done in the relevant area):

Presently we are working on the development of the novel fused heterocyclic compounds by applying new catalytic reagents and some of them have been mentioned below.

The present work with our research group involves the synthesis of novel biological active fused heterocycles containing imino/oxo pyrimdine ring fused through the nitrogen atom with another biologically active nucleus such as pyrazole, thiazole, benzothiazole and quinoline which is published in different reputed journals.

- Simple and efficient synthesis of substituted pyrimido [2,1-*b*][1,3] thiazines, Sambhaji P. Vartale et.al[1] ***Heterocyclic Communication*** 2013,19(3), 215-218.
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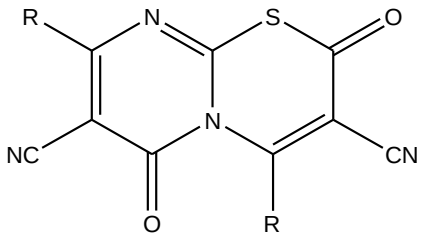
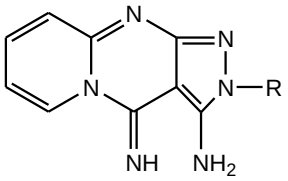
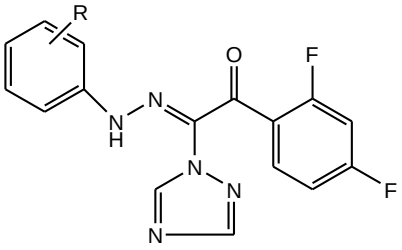


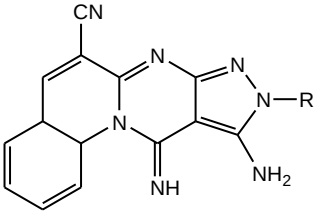
- An efficient synthesis of some novel 3-cyano-4-imino-2-(methylthio)-4H-pyrido[1,2-*a*]pyrimidine and their derivatives, Sambhaji P. Vartale ,et al.[2] ***J. Heterocyclic Chem,*** 2013, 50, 351-355.



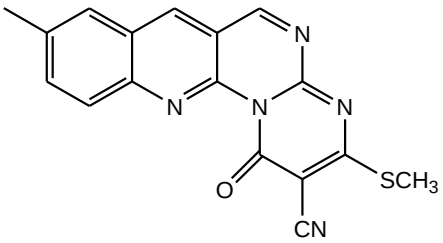

- Synthesis and biological activity of some fluorinated arylhydrazotriazoles, M.S.Shingare, S.A.Sadaphal et al.[3] ***Arabian Journal of Chemistry***, 2012 , 5, 257-261.



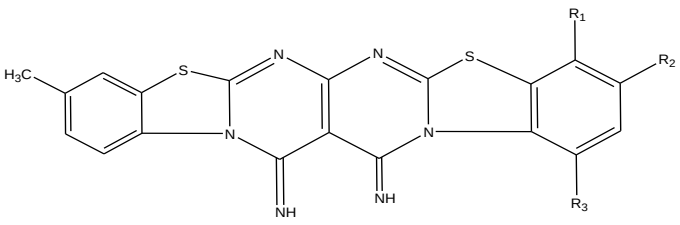

- Synthesis and Antimicrobial Evaluation of 3-amino-11- cyano-4-iminopyrazolo [4, 5-*e*]-4H-pyrimido [2,1-*b*]quinoline and their substituted derivatives. Sambhaji P.Vartale et al.[4] ***Heteroletter***, 2012,2, (1),71-78.



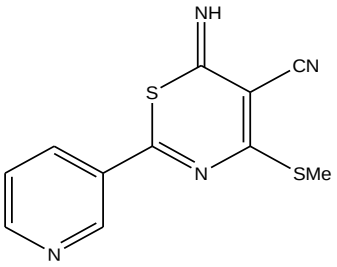

- Convenient one pot synthesis of 3-cyano-9-methylthio-4-oxo-4H-pyrimido[2,1-*b*] quinoline and its reactions with selected nucleophiles, Sambhaji P. Vartale et al.[5] ***Letters in Organic Chemistry***, 2009, 6(7), 544-548.




- A Convenient one pot synthesis and antimicrobial activity of 10-methyl-14,15-diimino benzothiazolo[2,3-*b*]pyrimido [5,6-*e*] pyrimido [2,3-*b*]benzothiazole and their substituted derivatives Sambhaji P.Vartale and Sharad V. Kuberkar et al[6] **Journals of *Pelagia Research Library***, 2011, 2(6), 46-51.



- Synthesis and antioxidant activity of 6-imino-4-(methylthio)-2-(pyridine-3-yl)-6H-1,3-thiazine-5-carbonitrile, Sambhaji P. Vartale et. al[7], **Journals of *International Research Journal of Pharmacy*** , DOI: 10.7897/2230-8407.089172.




## 3. Objectives of Research/ Proposed Hypothesis:

- Design synthesis of novel catalytic reagents.
- Extending the research of novel catalytic reagents to new domains, especially targeting the synthesis of different novel imino/oxo fused heterocyclic derivatives.
- Studying mechanistic details and pathways of novel catalytic reagents.
- Investigate the role of novel catalytic reagents in the activation of substances.
- Establishment of the structure of newly synthesized compounds with help of spectral data.
- Evaluation of physicochemical properties of synthesized novel imino/oxo fused heterocyclic compounds
- Evaluation of biological properties of synthesized novel imino/oxo fused heterocyclic compounds.

## 4. Methodology to be adopted:

- Literature Survey.
- Synthesis and conformation of structure of catalytic reagents.
- Synthesis and characterization of different imino/oxo fused heterocyclic derivatives by applying novel catalytic reagents.
- Characterization of newly synthesized heterocyclic compounds such as IR, $^{1}$H-NMR, $^{13}$C-NMR, Mass Spectroscopy.
- Study of physicochemical parameter of synthesized compounds.
- Evaluation of microbiological activities of synthesized compounds.
- Submission of data to International /National reputed journals for publication.

## 5. Importance of study/ Society application:

- **International Status:**

Nitrogen containing fused heterocyclic derivatives are to possess wide variety of biological properties. These compounds help in preventing many viral, fungal and bacterial disease as well as they acts as anti-tuberculosis and antioxidant drug with low toxicity. Because of the high efficiency of these compounds following research groups have recognized the importance of this field and made substantial contribution internationally.

1. **Yoshinori Yamamoto**
Department of Chemistry,
Graduate School of Science,
Tohoku University, Sendai 980-8578, **Japan.**

2. **Mohmud Sherif**
Department of Chemistry,
Faculty of Science,
Cairo University, Giza12613, **Egypt**.

3. **Tienan Jin,**
WPI-AIMR, Tohku University,
Katahira2-1-1, Aobaku,
Sendai 980-8577, **Japan.**

- **National Status:**

Nitrogen containing heterocycles such as pyrimidine, pyrazole, imidazole, quinoline are widely used in drug molecule these compounds act as antiviral, antifungal, anti-HIV, anticancer, antioxidant, anti-inflammatory agents with low toxicity. Because of the high efficiency of these compounds, following research groups have recognized the importance of this field and made significant contributions nationally.

1. **Dr. A. T. Bigu**
Organic Chemistry Division,
National Chemical Laboratory,
**Pune**, India

2**. Dr. N. T. Patil**
Organic Chemistry Division II,
Indian Institute of Chemical Technology,
**Hyderabad**-500 007, India

3. **Dr. D. S. Reddy**
Organic Chemistry Division,
National Chemical Laboratory,
**Pune**, India

- **Significance of the study:**

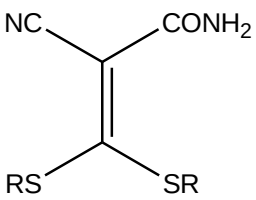
The investigation of novel antimicrobial drugs is an area characterized by vigorous exploration with the goal of overcoming the occurrence of multiple drug resistance. Fused heterocyclic rings like pyridine, pyrimidine, quinoline, thiazole, pyrazole, benzothiazole, were found to be biologically active compounds.

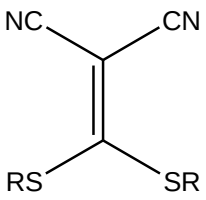
Fused hetero aromatic group containing sulfur, nitrogen, oxygen etc atoms play an important role as the hetero aromatic incorporated in to the structure of many pharmaceuticals.

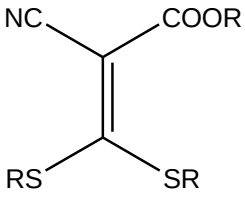
## 6. Proposed work plan/ Formulation and structure of study:

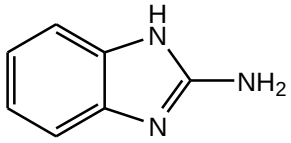
**a) Synthesis of amino heterocycles and reagents: (I$^{st}$Year)**

The proposed research work we plan to synthesize different ketene dithioacetals and different substituted amino heterocycles containing sulfur, nitrogen and oxygen as heteroatom.

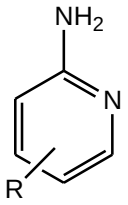


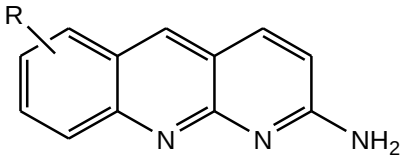



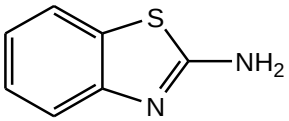

Substituted 2-Amino Benzimidazole




Substituted 2-amino pyridine




Substituted benzoquinolin-2-amine




Substituted 2-amino benzothiazole

**b) Condensation of synthesized amino heterocycles with different reagents: (II$^{nd}$ year)**

The synthesized amino heterocycles which contains more than one hetero atom as hetero atom condensation with reagent likes guanidine hydrochloride, thiourea and urea to synthesize main heterocyclic compounds.

Synthesized parent compound treated with different substituted aniline, phenol, heterylamine, active methylene compound will give new heterocyclic derivatives.

The above new parent pyrimido compound condensed with compound containing nitrogen atom like hydrazine hydrate, Hydrazeno heterocycles, carbonyl compounds to obtain new fused pyrazolo series derivatives.

Purification of synthesized compounds by using crystallization and conformation of structure by using spectral data.

**c) Evaluation of Physicochemical Parameters: (III$^{rd}$ Year**

Physicochemical study of heterocyclic compounds has very wide scope as this study can demonstrate how our synthesized compounds affect physical properties such as solubility, density, viscosity and refractive index.

**d) Evaluation of Biological Activity: (III$^{rd}$ Year)**

These above newly synthesized compounds are to be screened for their pharmacological properties like antioxidant, antimicrobial, antimalerial, antifungal, antituberculosis etc.

Hence, the present research work aimed to " **Synthesis, characterization of novel heterocyclic compounds using ketene thioacetals and evaluation of physicochemical properties with biological activities"**

## References:


**1.** Sambhaji P. Vartale et.al, *Heterocyclic Communication*, **2013**, 19(3), 215-218.

**2.** Sambhaji P. Vartale et al, *J. Heterocyclic Chem*., **2013**, 350-351.

**3.** M. S. Shingare, S.A.Sadaphal et al, *Arabian Journal of Chemistry* , **2012**, 5, 257-261.

**4.** Sambhaji P. Vartale et. al, *Heteroletter*, **2012**, 2(1), 71-78.

**5.** Sambhaji P. Vartale et al, *Letters in Organic Chemistry*, **2009**, 6(7), 544-548.

**6.** S.V. Kuberkar et al, *International Journal of Pharmaceutical, Chemical And Biological Science,* **2014**, 4(3), 660-664.

**7.** Sharad V. Kuberkar et al, *Journal of Chemical and Pharmaceutical Research*, **2012**, 4(3),1606-1611**.**

**8.** Sambhaji P. Vartale et al, *Research Journal of Recent Sciences,* **2017**, 6(2), 21-24.

**9**. Sambhaji P Vartale et al, *International Journal of Research in Pharmacy and Chemistry*, **2015**, 5(1), 208-214.

**10.** Sambhaji P. Vartale et al , *International Research Journal of Pharmacy*, **2017,** 160-164.

**11.** Sambhaji P. Vartale et al, *Heterocyclic Letters*, **2016**, 6(2), 275-281.s

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